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Surveillance for Safety After Immunization: Vaccine Adverse Event Reporting System (VAERS) — United States, 1991–2001

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Abstract

Problem/Condition: Vaccines are usually administered to healthy persons who have substantial expectations for the safety of the vaccines. Adverse events after vaccinations occur but are generally rare. Some adverse events are unlikely to be detected in prelicensure clinical trials because of their low frequency, the limited numbers of enrolled subjects, and other study limitations. Therefore, postmarketing monitoring of adverse events after vaccinations is essential. The cornerstone of monitoring safety is review and analysis of spontaneously reported adverse events.

Reporting Period Covered: This report summarizes the adverse events reported to the Vaccine Adverse Event Reporting System (VAERS) from January 1, 1991, through December 31, 2001.

Description of Systems: VAERS was established in 1990 under the joint administration of CDC and the Food and Drug Administration (FDA) to accept reports of suspected adverse events after administration of any vaccine licensed in the United States. VAERS is a passive surveillance system: reports of events are voluntarily submitted by those who experience them, their caregivers, or others. Passive surveillance systems (e.g., VAERS) are subject to multiple limitations, including underreporting, reporting of temporal associations or unconfirmed diagnoses, and lack of denominator data and unbiased comparison groups. Because of these limitations, determining causal associations between vaccines and adverse events from VAERS reports is usually not possible. Vaccine safety concerns identified through adverse event monitoring nearly always require confirmation using an epidemiologic or other (e.g., laboratory) study. Reports may be submitted by anyone suspecting that an adverse event might have been caused by vaccination and are usually submitted by mail or fax. A web-based electronic reporting system has recently become available. Information from the reports is entered into the VAERS database, and new reports are analyzed weekly. VAERS data stripped of personal identifiers can be reviewed by the public by accessing http://www.vaers.org. The objectives of VAERS are to 1) detect new, unusual, or rare vaccine adverse events; 2) monitor increases in known adverse events; 3) determine patient risk factors for particular types of adverse events; 4) identify vaccine lots with increased numbers or types of reported adverse events; and 5) assess the safety of newly licensed vaccines.

Results: During 1991–2001, VAERS received 128,717 reports, whereas >1.9 billion net doses of human vaccines were distributed. The overall dose-based reporting rate for the 27 frequently reported vaccine types was 11.4 reports per 100,000 net doses distributed. The proportions of reports in the age groups <1 year, 1–6 years, 7–17 years, 18–64 years, and ≥65 years were 18.1%, 26.7%, 8.0%, 32.6%, and 4.9%, respectively. In all of the adult age groups, a predominance among the number of women reporting was observed, but the difference in sex was minimal among children. Overall,

the most commonly reported adverse event was fever, which appeared in 25.8% of all reports, followed by injection-site hypersensitivity (15.8%), rash (unspecified) (11.0%), injection-site edema (10.8%), and vasodilatation (10.8%). A total of 14.2% of all reports described serious adverse events, which by regulatory definition include death, life-threatening illness, hospitalization or prolongation of hospitalization, or permanent disability. Examples of the uses of VAERS data for vaccine safety surveillance are included in this report.

Interpretation: As a national public health surveillance system, VAERS is a key component in ensuring the safety of vaccines. VAERS data are used by CDC, FDA, and other organizations to monitor and study vaccine safety. CDC and FDA use VAERS data to respond to public inquiries regarding vaccine safety, and both organizations have published and presented vaccine safety studies based on VAERS data. VAERS data are also used by the Advisory Committee on Immunization Practices and the Vaccine and Related Biological Products Advisory Committee to evaluate possible adverse events after vaccinations and to develop recommendations for precautions and contraindications to vaccinations. Reviews of VAERS reports and the studies based on VAERS reports during 1991–2001 have demonstrated that vaccines are usually safe and that serious adverse events occur but are rare.

Public Health Actions: Through continued reporting of adverse events after vaccination to VAERS by health-care providers, public health professionals, and the public and monitoring of reported events by the VAERS working group, the public health system will continue to be able to detect rare but potentially serious consequences of vaccination. This knowledge facilitates improvement in the safety of vaccines and the vaccination process.

Introduction

The National Childhood Vaccine Injury Act (NCVIA) (*1*) of 1986 required health professionals and vaccine manufacturers to report to the U.S. Department of Health and Human Services specific adverse events that occur after the administration of routinely recommended vaccines. Postvaccination adverse events and the time frames in which they must occur to qualify as being reportable under NCVIA are listed in the Reportable Events Table (*2*). The table is updated periodically as the vaccination schedule changes, new vaccines are introduced, and new vaccine-associated adverse events are identified. Vaccine-associated adverse event reports were previously collected separately by CDC and the Food and Drug Administration (FDA). CDC maintained the Monitoring System for Adverse Events Following Immunization (*3*) for vaccines administered in the public sector; FDA maintained the Spontaneous Reporting System (*4*) to accept reports from both the public and private sectors, although it was used primarily by vaccine manufacturers. These systems were replaced by the Vaccine Adverse Event Reporting System (VAERS) on November 1, 1990 (*5*). Under the joint administration of CDC and FDA, VAERS accepts spontaneous reports of suspected vaccine adverse events after administration of any vaccine licensed in the United States (*6–9*).

Unlike many surveillance systems that monitor a single exposure and its associated outcomes, VAERS monitors multiple exposures (i.e., different vaccines often administered simultaneously in different combinations) and an increasing number of potential outcomes. VAERS accepts spontaneous reports from health professionals, vaccine manufacturers, and the public. Reports are submitted by mail or fax. In 2002, electronic reporting to VAERS through the Internet became available by accessing http://secure.vaers.org/VaersDataEntryintro.htm. All reports, whether submitted directly to VAERS by an individual or by state or local public health authorities or manufacturers, are entered into the VAERS database.

Federal regulations require that each manufacturer with a product license from FDA report the following adverse events to VAERS: all spontaneous reports of adverse experiences occurring within the United States, whether serious, nonserious, expected or unexpected, and all serious and unexpected adverse experiences occurring outside of the United States or reported in scientific and medical journals as case reports or as the result of formal clinical trials (*10*). Data collected on the VAERS form (*11*) include information regarding the patient, the vaccine(s) administered, the reported adverse event, and the person reporting the event. Federal regulations (*10*) define serious events as those involving death, life-threatening illness, hospitalization or prolongation of hospitalization, or permanent disability. All reports with adverse events classified as serious are followed up with a request for additional information (e.g., medical records and autopsy reports) to provide a complete description of the case. For all original and follow-up reports, the signs, symptoms, and diagnoses mentioned in the description of the adverse event are coded using FDA's Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART) (*12*). All information is stored in a computerized database for subsequent reference and analyses. All reporters receive written acknowledgment of receipt of their reports along with a request for missing information where indicated. In addition, letters to obtain information regarding the recovery status of per-

sons with serious adverse events are mailed to the reporters at 60 days and 1 year after vaccination.

All personal identifying information is kept confidential as required by law. Medical records submitted to VAERS spontaneously or as part of follow-up activities are also protected by confidentiality requirements. VAERS data stripped of personal identifiers are available at http://www.vaers.org.

The primary objectives of VAERS are to 1) detect new, unusual, or rare vaccine adverse events; 2) monitor increases in known adverse events; 3) determine patient risk factors for particular types of adverse events; 4) identify vaccine lots with increased numbers or types of reported adverse events; and 5) assess the safety of newly licensed vaccines. Although VAERS can rarely provide definitive evidence of causal associations between vaccines and particular risks, its unique role as a national spontaneous reporting system enables the early detection of signals (*13*) that can then be more rigorously investigated. In vaccine safety surveillance, sensitivity takes precedence over specificity. VAERS seeks reports of any clinically important medical event that occurs after vaccination, even if the reporter cannot be certain that the event was caused by the vaccine.

The purpose of this report is to provide health-care providers, public health professionals, vaccine manufacturers, and members of the public who are interested in vaccine safety with an overview of the information collected in VAERS regarding adverse events reported during the previous 11 years. Specific examples of how the information was used to assess the safety of the vaccines and how VAERS detected signals that were later followed up are also included. Characterization of reporting profiles for different types of adverse events and vaccines also provides a context within which new and unexpected adverse events reported to VAERS can be interpreted.

Methods

The automated data in the VAERS database were used for analysis. All data were analyzed by using SAS® program version 8 (*14*). Unless otherwise indicated, only reports received from January 1, 1991, through December 31, 2001, were included. All known duplicate reports (reports concerning the same patients but from different reporting sources) were excluded.

All adverse events in the VAERS database were coded using COSTART (*12*). Reports typically involve multiple COSTART coding terms. Serious adverse events were defined by the federal regulatory definition for seriousness (*10*), which includes information regarding whether the patient died, experienced life-threatening illness, required hospitalization, and whether the condition resulted in prolongation of hospitalization or in permanent disability.

The numbers of adverse event reports in each of the 50 states were calculated by year. The average reporting rates (reports per 1 million population) for each state were calculated by dividing the averages of 11 annual reports of each state by the averages of 1990 and 2000 state population data from the Bureau of the Census.

The vaccine-specific reporting rates for each vaccine type (number of reports per 100,000 net doses distributed) were calculated by dividing the number of vaccine-specific reports by the net doses distributed in the United States, according to the data provided by the CDC Biologics Surveillance System (personal communication, Lisa Galloway, National Immunization Program, 2002) (Table 1). These data were provided by the majority of vaccine manufacturers by type of antigen and year of distribution. These net distribution figures are only estimates and serve as approximate denominators for reporting rates of adverse events in the absence of data regarding actual number of doses administered. Net distribution figures represent the total doses distributed by vaccine type during the period, less returned doses. The reporting rates must not be interpreted as incidence rates because whether the vaccine caused the adverse event was uncertain. The adverse event might have occurred by chance after vaccination. In addition, substantial and variable underreporting occurs, and uncertainty exists regarding the actual number of doses administered.

The numbers of adverse event reports were calculated in five age groups: <1 year, 1–6 years, 7–17 years, 18–64 years, and ≥65 years. The unknown age group was defined as not being able to determine age because of missing information.

The frequently reported vaccine types or vaccine combinations were defined as vaccine types or vaccine combinations for which ≥50 adverse event case reports were received. The frequently reported adverse events were defined as the COSTART coding terms of adverse events that were reported ≥100 times.

Results

Summary of VAERS Data

General

From January 1, 1991, through December 31, 2001, VAERS received 128,717 case reports describing adverse events after immunization. This report includes data regarding the distribution of these reports by year and the population-based reporting rates in the 50 states (Table 2). The reporting rates

varied from 27.7 (Alabama) to 113.2 (Alaska) reports per million population. The four most populous states in the United States (California, Florida, Texas, New York) had low reporting rates of 28.4, 30.3, 32.0, and 35.8, respectively. In contrast, the states with the highest reporting rates were Alaska (113.2), Idaho (81.4), and Wyoming (75.2), which are some of the least populated states.

Data regarding the number of adverse event reports for each of the 27 frequently reported vaccine types are included in this report (Table 3). During 1991–2001, >1.9 billion net doses of human vaccines were distributed (Table 1), resulting in an overall dose-based reporting rate for the 27 vaccine types of 11.4 reports per 100,000 net doses distributed. The influenza vaccine (FLU) had the highest distribution (>500 million doses) but the lowest overall reporting rate (3.0 reports per 100,000 net doses distributed). Hepatitis B (HEP) vaccine had the second highest distribution (>200 million net doses) but an overall reporting rate of 11.8 reports per 100,000 net doses distributed. Rhesus rotavirus vaccine-tetravalent (RRV-TV) had the highest overall reporting rate for a specific vaccine (156.3 reports per 100,000 net doses distributed). Two major vaccine substitutions occurred during the 11-year period: diphtheria and tetanus toxoids and acellular pertussis (DTaP) replaced diphtheria and tetanus toxoids and pertussis vaccine (DTP), and inactivated poliovirus vaccine (IPV) replaced oral poliovirus vaccine live trivalent (OPV) for routine vaccinations. The overall reporting rate has decreased substantially after vaccination with DTaP (12.5 reports per 100,000 net doses distributed), compared with that for DTP (26.2). A similar, though limited decrease in average reporting rate was also observed after vaccination with IPV (13.1), compared with that for OPV (15.1) after transition from OPV to IPV in 1996.

During the 11-year surveillance period, 44.8% of all reports involved children aged <7 years (<1 year: 18.1% and 1–6 years: 26.7%) (Table 4). The recommended vaccination schedules primarily involve these age groups. A total of 32.6% of all reports were for adults aged 18–64 years, and 4.9% concerned adults aged ≥65 years. Among children, the difference in sex was minimal in all age groups (<1 year, 1–6 years, and 7–17 years) (Figure 1). In contrast, an excess of reports for women was noted for all adult age groups (18–64 years and ≥65 years) throughout the surveillance period.

Changes in reporting frequencies of different vaccines or vaccine combinations examined by comparing data from two surveillance periods are included in this report (Tables 5 and 6). During the earlier period, 1991–1995, >74% of all VAERS reports mentioned the use of HEP; FLU; measles, mumps, and rubella (MMR); DTP; or tetanus and diphtheria toxoids (Td) vaccines and combined use of DTP with *Haemophilus* b conjugate virus vaccine (HIBV), OPV, HEP, and MMR (Table 5). Because of the introduction of multiple new vaccines and vaccine combinations and changes in the recommended immunization schedules, the reporting pattern in VAERS changed during the latter period, 1996–2001. Although HEP, FLU, Td, and MMR remained among the most frequently reported vaccines, a substantial number of reports followed the use of varicella (VARCEL), pneumococcal (PPV), anthrax (ANTH), and Lyme disease vaccines (LYME) as well as acellular pertussis vaccines administered either alone or in combination with HEP, HIBV, IPV and/or MMR (Table 6).

Overall, the most commonly reported adverse event was fever, which appeared in 25.8% of all reports, followed by injection-site hypersensitivity (15.8%), rash (unspecified) (11.0%), injection-site edema (10.8%), and vasodilatation (COSTART coding term for skin redness) (10.8%) (Table 7). At least one of these primarily nonserious adverse events was mentioned in 74.2% of all VAERS reports.

VAERS reports were received primarily from vaccine manufacturers (36.2%), state and local health departments (27.6%), and health-care providers (20.0%), with fewer reports filed directly by patients and parents (4.2%), or others (7.3%) (Table 8). Data documented a continuous increase in the proportion of reporting by health-care providers during the 11-year period. The percentage of reports from health-care providers increased from 11.4% in 1991 to 35.3% in 2001. The improvement in reporting from health-care providers might reflect the efforts of the VAERS working group to enhance communication with physicians through yearly direct mailing, continuing medical education (CME), and other sources. In addition, publications of analyses of VAERS data might have increased health-care providers' recognition of the potential value of reporting.

Serious Adverse Events

Overall, 14.2% of all reports received in VAERS during 1991–2001 described serious adverse events (*10*) (Table 9). During 1991–2001, reports of deaths ranged from 1.4%–2.3%, and reports of life-threatening illness ranged from 1.4%–2.8% of all adverse event reports. During the previous 3 years when distribution of vaccines reached the highest level, the annual percentage of reports of death was stable, approximately 1.5% of all adverse event reports. The reports of life-threatening illness were also stable throughout the years except for a peak of 2.8% in 1999, which reflected RRV-TV and intussusception incident that occurred in that year.

A clinical research team follows up on all deaths reported to VAERS. The majority of these deaths were ultimately classified as sudden infant death syndrome (SIDS). Analysis of the age distribution and seasonality of infant deaths reported to

VAERS indicated that they matched the age distribution and seasonality of SIDS; both peaked at aged 2–4 months and during the winter (*15*). The decrease in deaths reported to VAERS since 1992–1993 parallels the overall decrease in SIDS in the U.S. population since the implementation of the Back to Sleep campaign (*15*). Carefully controlled epidemiologic studies consistently have not found any association between SIDS and vaccines (*16–19*). FDA and the Institute of Medicine (IOM) reviewed 206 deaths reported to VAERS during 1990–1991. Only one death was believed to have resulted from a vaccine. The patient was a woman aged 28 years who died from Guillain-Barré syndrome after tetanus vaccination (*20*). IOM concluded that the majority of deaths reported to VAERS are temporally but not causally related to vaccination (*20*). A similar conclusion was reached regarding neonatal deaths temporally reported to VAERS in association with hepatitis B vaccination (*21*).

VAERS in Vaccine Safety Surveillance

Intussusception After Rotavirus Vaccine

RRV-TV was licensed in August 1998. The Advisory Committee on Immunization Practices (ACIP) recommendations for its use were published in March 1999 (*22*). From September 1, 1998, through July 7, 1999, VAERS received 15 reports of intussusception among infants who had received RRV-TV vaccine. CDC reported this finding in July 1999 and recommended that health-care providers postpone use of RRV-TV at least until November 1999, pending results of a national case-control study that was being conducted at that time (*23*). The manufacturer, in consultation with FDA, voluntarily ceased further distribution of the vaccine in mid-July 1999. On October 22, after a review of scientific data from multiple sources, ACIP concluded that intussusception occurred with substantially increased frequency in the first 1–2 weeks after vaccination with RRV-TV, particularly after the first dose. In 1999, ACIP withdrew its recommendation for vaccination of infants in the United States with RRV-TV (*24*).

From September 1998 through December 1999, VAERS received 121 reports of intussusception among infants who received RRV-TV vaccine (Figure 2). The first intussusception case was reported in December 1998. During the first half of 1999, a total of 14 additional cases of intussusception were reported to VAERS. The majority of cases were reported during July–August 1999, peaking soon after a MMWR publication (July 16, 1999) (*23*). Other studies have documented similar findings (*25–29*). All intussusception case-patients reported to VAERS through December 31, 1999, were vaccinated before July 17, 1999 (Figure 3). Before RRV-TV was licensed and marketed in the United States, VAERS had received a total of only three reports of intussusception after other vaccinations (Figure 4).

Influenza Vaccine and Guillain-Barré Syndrome

Vaccination with swine influenza vaccine is known to increase the risk for Guillain-Barré syndrome (*30–34*). Reports of Guillain-Barré syndrome after any vaccination are considered serious and followed up by VAERS to obtain additional information. An increase in reports of Guillain-Barré syndrome after the receipt of influenza vaccine was noted in VAERS data by week 29 of the 1993–94 influenza season (*35*). The number of reports increased from 23 during 1991–92 to 40 during 1992–93 and to 80 during 1993–94 (Figure 5). These findings raised concerns regarding a possible increase in vaccine-associated risk for Guillain-Barré syndrome. A study was initiated to investigate the VAERS signal (*35*). The study documented that the relative risk of Guillain-Barré syndrome after influenza vaccination, adjusted for age, sex, and vaccine season was 1.7 (95% confidence interval = 1.0–2.8). However, no increase occurred in the risk of vaccine-associated Guillain-Barré syndrome from 1992–93 to 1993–94. For the two seasons combined, the adjusted relative risk of 1.7 indicated that slightly >1 additional case of Guillain-Barré syndrome occurred per 1 million persons vaccinated against influenza. This risk is less than the risk from severe influenza, which can be prevented by the vaccine. In addition, no correlation existed between the number of Guillain-Barré syndrome reports received in VAERS and influenza vaccine doses administered (Figure 5). The annual number of Guillain-Barré syndrome reports has been low and stable during the previous four influenza seasons when the net doses of influenza vaccine distributed increased substantially. This finding reflects data compared with the 1993–94 influenza season in which VAERS received the highest numbers of Guillain-Barré syndrome reports in a single influenza season. This example indicates that VAERS is useful in preliminary evaluation of rare adverse events when the relation to vaccination is uncertain.

Safety Assessment After Whole Cell Versus Acellular Pertussis-Containing Vaccines

Concerns regarding the safety of DTP vaccines led to a gradual introduction of acellular pertussis-containing vaccines in the United States. In December 1991, FDA licensed the first DTaP vaccine for use in the United States (*36*). Shortly thereafter, a second DTaP formulation was also licensed (*37*). Both DTaP vaccines were licensed for use only as the fourth and fifth doses of the DTP series recommended for children

aged 15 months–7 years. In July 1996, FDA approved the first DTaP vaccine for infants (*38*).

VAERS reports from 1991 (when whole cell pertussis vaccines were used exclusively) through 2001 (when acellular pertussis vaccines were used predominantly) documented that the overall vaccine-specific reporting rates of both serious and nonserious reports for DTaP had decreased to less than one half of that for DTP among children aged <7 years (Table 10). In comparison with all whole cell pertussis-containing vaccines (DTP and DTPH), the overall nonserious adverse events reporting rate for DTaP vaccines was approximately 40% lower (10.5 versus 16.8 reports per 100,000 net doses distributed). Although reduction in adverse reporting rates is suggestive of a safer vaccine, such comparisons must be interpreted cautiously because reporting rates cannot be viewed as incidence rates. Two studies have documented an improved safety profile of DTaP vaccines based on review of VAERS data from 1991–1993 among children and 1995–1998 among infants (*39,40*). The decreasing trends for selected systemic adverse events (e.g., fever) and neurologic reactions (e.g., seizures) continued to be observed during 1999–2001 (Figures 6 and 7). However, an increase in the number of reports concerning injection-site reactions was detected by the end of this surveillance period (Figure 8). The increase is more prominent among the recipients of booster doses of DTaP (fourth and fifth dose). This finding is consistent with the results of a recent study that documented an increase in the risk of extensive local reactions in recipients of fourth and fifth doses of the DTaP vaccines (*41*).

Safety Assessment After IPV Versus OPV

Since it was licensed in 1963, OPV has been the vaccine used for the prevention of poliovirus infection in the United States. The use of OPV led to the elimination of wild-type poliovirus in the United States in <20 years. However, the risk of vaccine-associated paralytic poliomyelitis (VAPP) was estimated to be approximately 1 case per 2.4 million doses distributed, with the majority of VAPP cases occurring after the administration of the first dose (1 case per 750,000 first doses) (*42,43*). The reporting sensitivity of VAPP in VAERS was an estimated 68%–72% (*44*). In September 1996, to reduce the occurrence of VAPP, ACIP recommended an increase in the use of IPV through a sequential schedule of IPV followed by OPV (*42*). VAERS has not received any report of VAPP after OPV/IPV vaccination since 1997, suggesting a positive effect of the sequential schedule of IPV followed by OPV (Figure 9). This result is consistent with previously reported data (*45*). In July 1999, ACIP recommended that IPV be used exclusively in the United States to maintain disease elimination and to prevent any further cases of VAPP (*46*).

Safety Assessment After Varicella Vaccine

In March 1995, varicella vaccine was licensed in the United States. In July 1996, varicella vaccine was recommended by ACIP for all children without contraindications at aged 12–18 months, for all susceptible children by their thirteenth birthday, and for susceptible adolescents and adults who are at high risk for exposure to varicella (*47*). In February 1999, ACIP expanded its recommendations for varicella vaccine to promote an expanded use of the vaccine for susceptible children and adults (*48*).

VAERS received 15,180 adverse event reports after varicella vaccination from March 1995 through December 2001, the majority (14,421, or 95%) of which described nonserious events. The highest numbers of reports were received soon after licensure (Figure 10). As the net distribution of varicella vaccine increased, the number of adverse event reports decreased continuously over the years. Of the 15,180 adverse event reports received, the number of serious adverse events reported for varicella vaccine was 759 (5%). The proportion of reports of serious adverse events was stable over the years (range: 3.7%–6.3%).

A detailed review of VAERS reports received during the first 3 years after the licensure of varicella vaccine documented that the majority of reported adverse events for varicella vaccine were minor, and serious events were rare (*49*). A vaccine etiology for the majority of reported serious events could not be confirmed; further research is needed to clarify whether varicella vaccine played a role.

Safety Assessment After Lyme Disease Vaccine

In December 1998, FDA licensed the first vaccine to prevent Lyme disease. ACIP stated that the vaccine should be considered for persons who reside in areas where Lyme disease is endemic and who have frequent or prolonged exposure to tick-infested habitats (*50*). Review of early reports to VAERS revealed adverse events that corresponded to Lyme vaccine safety data from the prelicensure trials, including injection-site reactions, transient arthralgia and myalgia within 30 days of vaccination, fever, and flu-like symptoms. Hypersensitivity reactions, not observed in the clinical trial, were also reported to VAERS. Some of the reported hypersensitivity reactions can be linked to the vaccine on the basis of the specificity of the symptoms, close temporal proximity to

vaccination, and the known association of the reactions with other vaccines. For other reported adverse events, causal relations with Lyme disease vaccine have not been established. No clear patterns in age, sex, time to onset, or vaccine dose have been identified. The onset of symptoms consistent with Lyme disease (e.g., facial paralysis and arthritis) after Lyme disease vaccination has also been reported to VAERS. Determining whether the facial paralysis was part of the expected background incidence or attributable to the vaccine or to Lyme disease was not possible. A higher proportion of arthritis-related events was reported after the second or third dose compared with all events combined. This higher proportion might be attributable to the increased amount of time available for a vaccine recipient to report an adverse event: 11 months between the second and third doses (*51*). Because of persistent public concerns, a follow-up study was conducted to further evaluate reports of arthritis after vaccination for Lyme disease. In 7 of 14 confirmed arthritis cases, a history of concomitant exposure or another medical condition existed, including Lyme disease, that provided a possible explanation for arthritis (*52*). In early 2001, the manufacturer withdrew the vaccine from the market, citing poor sales.

Discussion

This report provides an overview of reports to VAERS during 1991–2001. The VAERS data should be interpreted with caution, because they describe events that occurred after vaccination but they do not necessarily imply that the events were caused by vaccination. Although the 128,717 adverse event reports received in VAERS during the previous 11 years are a substantial number, it is low in comparison with the >1.9 billion doses of vaccines administered in the United States during the same period (Table 1). VAERS seeks to capture as many clinically important medical events after vaccination as possible, even if the person who reported the event was not certain that the incident was vaccine-related. Temporal association alone does not mean that the vaccine caused the illness or symptoms. The illness or symptoms could have been a coincidence or might have been related to an underlying disease or condition or might have been related to medicines or other products taken concurrently.

During 1999–2001, more reports were submitted to VAERS annually than in the early 1990s. Multiple factors that likely contributed to this increase include the introduction of new vaccines in the mid- to late 1990s (rotavirus vaccine, Lyme disease vaccine, varicella vaccine, and pneumococcal conjugate vaccine), the increased use of anthrax vaccine by military personnel, and the increase in the number of doses of vaccines administered to both adult and children (Table 1). In addition, reporters have become increasingly aware of VAERS.

Because of the diverse population VAERS covers and the number of reports it receives, VAERS is useful for detecting new, unusual, or rare events and assessing newly licensed vaccines. Review of reports during the initial months of licensed use of a new vaccine cannot only rapidly identify problems not detected during prelicensure evaluation (e.g., intussusception and RRV-TV) but also reassure the general public concerning the safety of a new vaccine, as in the safety assessments of varicella vaccine and hepatitis A (HEPA) vaccine (*53*). VAERS has also been useful in screening for unusual increases in previously reported adverse events (e.g., influenza vaccine and Guillain-Barré syndrome investigation during the 1992–93 and 1993–94 influenza seasons).

Investigating changes in reporting rates in VAERS might lead to positive change in vaccine practices. After the licensure of DTaP for the fourth and fifth doses in the vaccination schedule of older children, VAERS data were used to compare reporting rates for specific adverse events after DTaP versus DTP within the first 72 hours after vaccination (*39*). This study confirmed a better safety record for DTaP among older children and was one factor in ACIP's subsequent recommendation for the use of DTaP among infants. As was also critical in the safety assessment of IPV versus OPV, VAERS provided evidence of improved safety in evaluating changes in immunization practices recommended by ACIP.

VAERS has also facilitated the lot-specific safety evaluations, which have periodically been of public concern. Lot sizes vary substantially. Every lot of vaccine must meet strict criteria for purity, potency, and sterility before it can be released to the public by the manufacturer. FDA medical officers review all reports of death and other serious events, and they also look each week for clusters within the same vaccine lot. In addition, FDA medical officers evaluate reporting rates of adverse events by lot, as needed, looking for unexpected patterns. During the 11 years, no lot needed to be recalled on this basis.

VAERS is subject to the limitations inherent in any passive surveillance system (*54*). Among those, underreporting (only a fraction of the total number of potentially reportable events occurring after vaccination are reported) and differential reporting (more serious events and events with shorter onset time after vaccinations are more likely to be reported than minor events) are most noticeable (*44*). Overreporting also occurs because certain reported adverse events might not be caused by vaccines, and some reported conditions do not meet standard diagnostic criteria. Many reported events, including serious ones, might occur coincidentally after vaccination and are not causally related to vaccination. Other potential

reporting biases include increased reporting in the first few years after licensure, increased reporting of events occurring soon after vaccination, and increased reporting after publicity about a particular known or alleged type of adverse event. Individual reports might contain inaccurate or incomplete information. Because of all of these reasons as well as the absence of control groups, differentiating causal from coincidental conditions by using VAERS data alone usually is not possible. Other methodologic limitations of VAERS include the fact that it does not provide information regarding background incidence of adverse events in the general population nor does it provide information concerning the total number of doses of vaccine or vaccine combinations actually administered to patients.

Despite its limitations, VAERS contributes to public health in critical ways. CDC and FDA have published and presented numerous vaccine safety studies based on the analyses of VAERS data (*55*). The high number of reports and the national coverage increase the possibility of detecting or better understanding adverse events that might occur too rarely to be considered as a signal in prelicensure clinical trials or even in a postmarketing active surveillance program. The identification of signals by monitoring VAERS data might initiate further investigation of potential problems in vaccine safety or efficacy and subsequent dissemination of safety-related information to the scientific community and the public. VAERS is also used to evaluate the safety of vaccines used in unique populations (e.g., travelers and the military). Studies have been published regarding Japanese encephalitis (*56*), Lyme (*51*), meningococcal (*57*), and yellow fever vaccines (*58,59*), among others.

To provide a more rigorous setting in which investigators can follow up on signals from VAERS or concerns arising from other sources, the Vaccine Safety Datalink (VSD) Project, a large-linked database, was established in 1991 (*60*). VSD includes information concerning >7 million persons in eight health maintenance organizations (HMOs) throughout the United States. The strengths of VSD include the documentation of immunizations, the absence of underreporting bias of medical outcomes, and the inclusion in the database of a high number of vaccinated persons who did not have adverse events. However, the VSD data are not available for analysis in as timely a manner as the VAERS data and are not fully representative of the U.S. population regarding race, socioeconomic status, health-care setting, or vaccine lot uses. Nonetheless, VSD permits the conducting of planned epidemiologic vaccine safety studies as well as, in certain situations, urgent investigations of new hypotheses (*28*).

In addition to VSD, CDC has established a new collaborative project, the national network of Clinical Immunization Safety Assessment (CISA) Centers. The centers will develop and disseminate standardized clinical evaluation protocols to clinicians. In addition, the CISA centers will provide referral and consultation services to health-care providers regarding the evaluation of patients who might have had an adverse reaction to vaccination, which will include how to manage the adverse reaction and provide counsel on advisability of continued vaccination. The CISA centers will undertake outreach and educational interventions in the area of vaccination safety. The objectives of CISA are to enhance understanding of known serious or unusual vaccine reactions, including the pathophysiology and risk factors for such reactions, as well as to evaluate newly hypothesized syndromes or events identified from the assessment of VAERS data to clarify any potential relation between the reported adverse events and immunization. Certain adverse events are rarely seen in clinical trials, and clinicians see them too rarely to manage them in a standardized manner. CISA will fill this gap by assisting clinicians in the management of adverse events after immunization.

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Vaccine Codes* Used in the Vaccine Adverse Event Reporting System (VAERS)

Vaccine Code	Description
ANTH	Anthrax vaccine adsorbed
DT	Diphtheria and tetanus toxoids adsorbed
DTAP	Diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed
DTP	Diphtheria and tetanus toxoids and pertussis vaccine adsorbed
DTPH	Diphtheria and tetanus toxoids and pertussis vaccine adsorbed and *Haemophilus* b conjugate vaccine (diphtheria CRM197 protein conjugate)
FLU	Influenza virus vaccines
HBHEPB	*Haemophilus* b conjugate vaccine and hepatitis B vaccine (recombinant)
HEP	Hepatitis B vaccines (recombinant)
HEPA	Hepatitis A vaccines inactivated
HIBV	*Haemophilus* b conjugate vaccines
IPV	Inactivated poliovirus vaccine
JEV	Japanese encephalitis virus vaccine inactivated
LYME	Lyme disease vaccine (recombinant OspA)
M	Measles virus vaccine live
MEN	Meningococcal polysaccharide vaccine
MMR	Measles, mumps, and rubella virus vaccine live
OPV	Oral poliovirus vaccine live trivalent (sabin strains types 1, 2 and 3)
PNC	Pneumococcal 7-valent conjugate vaccine (diphtheria CRM197 protein)
PPV	Pneumococcal vaccines, polyvalent
R	Rubella virus vaccine live
RAB	Rabies vaccines
RV	Rotavirus vaccine live, oral, tetravalent
TD	Tetanus and diphtheria toxoids adsorbed for adult use
TTOX	Tetanus toxoid
TYP	Typhoid vaccines
VARCEL	Varicella virus vaccine live
YF	Yellow fever vaccine

*Vaccine codes used in VAERS for vaccine types, which might represent multiple similar vaccines made by different vaccine manufacturers.

TABLE 1. CDC biologics surveillance data* — United States, 1991–2001

Vaccine types§	Total net doses distributed†											
	Year											
	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	Total
ANTH¶	—**	—	—	—	—	—	—	481,515	996,638	481,514	25,987	**1,985,654**
DT	1,384,390	1,377,432	1,800,499	1,079,191	1,338,871	1,090,017	573,267	690,465	443,702	336,987	428,140	**10,542,961**
DTAP	—	1,708,228	3,907,915	4,706,165	4,939,410	6,830,615	14,874,775	16,707,325	19,848,959	17,355,117	17,955,984	**108,834,493**
DTP	19,341,055	19,502,535	16,667,844	7,754,229	5,246,313	3,632,971	474,127	257,155	466,360	152,556	67,903	**73,563,048**
DTPH	—	—	3,210,340	12,013,470	12,650,370	11,291,600	5,656,830	2,573,220	834,564	—	—	**48,230,394**
DTaP-HIB††	—	—	—	—	—	—	528,273	602,880	645,458	690,171	453,534	**2,920,316**
FLU	32,809,662	40,352,367	42,980,814	60,084,728	36,512,538	38,915,520	40,996,883	48,080,122	60,468,427	65,582,650	61,953,006	**528,736,717**
HBHEPB	—	—	—	—	—	—	882,606	1,850,319	2,935,569	4,754,165	5,230,135	**15,652,794**
HEP	3,555,775	20,404,964	32,777,217	31,200,758	16,595,241	22,030,609	28,395,242	34,394,128	30,437,611	28,013,544	28,698,635	**276,503,724**
HEPA	—	—	—	—	3,823,000	2,302,925	3,487,445	4,256,114	4,151,283	6,426,621	7,258,381	**31,705,769**
HIBV	16,862,932	15,076,004	12,848,397	8,145,126	5,272,618	4,438,343	9,573,546	12,531,386	13,698,620	11,383,516	9,431,417	**119,261,905**
IPV	103,436	275,376	281,257	347,656	448,030	1,275,537	5,228,097	6,048,082	10,420,168	17,712,225	18,119,320	**60,259,184**
JEV	—	—	41,695	174,629	162,925	162,093	175,956	101,312	135,918	139,708	104,643	**1,198,879**
LYME§§									967,000	428,000	93,000	**1,488,000**
M	1,138,740	493,290	406,566	279,902	184,294	205,113	135,083	134,909	107,736	83,764	94,403	**3,263,800**
MEN	58,842	385,035	400,523	624,714	859,195	532,677	710,168	997,430	723,096	1,296,864	1,424,442	**8,012,974**
MMR	13,662,657	13,399,606	13,388,958	15,281,375	13,614,411	11,091,265	13,188,702	13,822,162	13,896,719	12,682,704	11,552,532	**145,581,091**
OPV	19,052,840	19,411,620	18,992,060	22,606,350	20,700,000	18,516,650	12,595,000	11,740,830	10,072,300	—	—	**153,287,650**
PNC	—	—	—	—	—	—	—	—	—	13,663,100	15,256,865	**28,919,965**
PPV	2,713,281	2,555,262	3,597,095	4,492,680	4,927,380	7,103,615	6,825,035	7,781,485	7,037,540	7,056,265	4,358,078	**58,447,716**
R	363,826	321,261	300,610	280,397	294,170	289,131	299,238	288,615	315,635	241,295	259,707	**3,253,885**
RAB	168,166	191,716	118,272	223,813	247,545	236,819	265,362	227,275	249,558	155,822	200,752	**2,285,100**
RV	—	—	—	—	—	—	—	—	453,120	—	—	**453,120**
TD	12,452,950	12,991,037	15,189,664	17,151,343	13,872,190	12,667,682	15,235,446	15,987,245	13,693,807	12,539,325	11,000,458	**152,781,147**
TTOX	4,016,110	3,407,521	3,208,265	2,893,330	2,632,505	1,678,600	1,436,824	1,599,110	1,902,657	1,367,046	909,777	**25,051,745**
TYP	—	—	—	—	—	—	192,902	564,400	1,144,922	1,368,040	1,099,159	**4,369,423**
VARCEL	—	—	—	—	1,140,449	2,685,538	3,736,938	5,323,008	5,526,977	6,164,324	5,787,866	**30,365,100**
YF	134,270	668,875	247,255	898,680	725,415	724,695	671,875	718,185	602,227	533,065	502,162	**6,426,704**
Total	**127,818,932**	**152,522,129**	**170,365,246**	**190,238,536**	**145,786,858**	**147,702,015**	**166,139,620**	**187,758,677**	**202,176,571**	**210,608,388**	**202,266,286**	**1,903,383,258**

* Personal communication, Lisa Galloway, National Immunization Program, 2002.

† Total net doses of vaccine distributed equals the total doses distributed by vaccine type and by year, less the doses returned.

§ The Vaccine Adverse Event Reporting System (VAERS) coding terms for vaccine types. See the Vaccine Codes Used in the Vaccine Adverse Event Reporting System (VAERS) section of this report for a description of each coding term.

¶ Data provided by the Department of Defense.

** Data not available.

†† Not a VAERS coding term; represents the combination product of DTaP and HIBV.

§§ Not licensed until December 1998; data provided by the vaccine manufacturer.

TABLE 2. Vaccine Adverse Event Reporting System (VAERS) reports and population-based reporting rates in the 50 states — United States, 1991–2001

State	1991		1992		1993		1994		1995		1996		1997	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
AK	46	0.5	61	0.6	54	0.5	47	0.5	62	0.6	68	0.6	45	0.4
AL	115	1.1	222	2.1	90	0.9	119	1.1	105	1.0	85	0.8	120	1.0
AR	122	1.2	90	0.8	146	1.4	137	1.3	131	1.3	124	1.1	151	1.3
AZ	105	1.0	105	1.0	112	1.1	116	1.1	136	1.3	155	1.4	149	1.3
CA	661	6.6	804	7.4	827	8.0	849	8.2	892	8.7	908	8.1	864	7.4
CO	186	1.9	197	1.8	158	1.5	182	1.8	181	1.8	245	2.2	193	1.6
CT	87	0.9	102	0.9	145	1.4	127	1.2	126	1.2	124	1.1	136	1.2
DC	36	0.4	23	0.2	36	0.3	39	0.4	24	0.2	39	0.3	36	0.3
DE	27	0.3	28	0.3	28	0.3	36	0.3	24	0.2	21	0.2	29	0.2
FL	311	3.1	403	3.7	379	3.7	392	3.8	421	4.1	436	3.9	459	3.9
GA	489	4.9	330	3.0	293	2.8	305	2.9	320	3.1	320	2.8	324	2.8
HI	35	0.3	67	0.6	33	0.3	54	0.5	37	0.4	60	0.5	40	0.3
IA	220	2.2	136	1.3	118	1.1	95	0.9	104	1.0	105	0.9	134	1.1
ID	78	0.8	95	0.9	102	1.0	123	1.2	70	0.7	106	0.9	86	0.7
IL	382	3.8	346	3.2	372	3.6	403	3.9	375	3.6	419	3.7	388	3.3
IN	169	1.7	144	1.3	212	2.1	154	1.5	180	1.7	155	1.4	173	1.5
KS	128	1.3	129	1.2	107	1.0	110	1.1	119	1.2	115	1.0	111	0.9
KY	115	1.1	143	1.3	75	0.7	89	0.9	59	0.6	89	0.8	91	0.8
LA	161	1.6	128	1.2	117	1.1	130	1.3	127	1.2	126	1.1	112	1.0
MA	160	1.6	246	2.3	315	3.1	298	2.9	276	2.7	329	2.9	414	3.5
MD	272	2.7	243	2.2	211	2.0	204	2.0	236	2.3	276	2.5	256	2.2
ME	32	0.3	72	0.7	106	1.0	72	0.7	62	0.6	61	0.5	79	0.7
MI	354	3.5	391	3.6	445	4.3	389	3.8	372	3.6	456	4.1	459	3.9
MN	186	1.9	216	2.0	226	2.2	191	1.8	205	2.0	243	2.2	269	2.3
MO	220	2.2	212	2.0	218	2.1	255	2.5	204	2.0	257	2.3	224	1.9
MS	94	0.9	112	1.0	95	0.9	112	1.1	85	0.8	90	0.8	89	0.8
MT	32	0.3	48	0.4	49	0.5	48	0.5	36	0.3	41	0.4	48	0.4
NC	273	2.7	314	2.9	264	2.6	260	2.5	308	3.0	338	3.0	272	2.3
ND	19	0.2	36	0.3	37	0.4	38	0.4	54	0.5	47	0.4	44	0.4
NE	59	0.6	65	0.6	62	0.6	53	0.5	79	0.8	79	0.7	103	0.9
NH	117	1.2	93	0.9	70	0.7	82	0.8	77	0.7	91	0.8	74	0.6
NJ	324	3.2	299	2.8	298	2.9	344	3.3	310	3.0	348	3.1	309	2.6
NM	81	0.8	50	0.5	58	0.6	57	0.6	62	0.6	79	0.7	66	0.6
NV	41	0.4	31	0.3	62	0.6	45	0.4	76	0.7	54	0.5	58	0.5
NY	491	4.9	582	5.4	590	5.7	616	5.9	624	6.1	744	6.6	731	6.2
OH	330	3.3	358	3.3	404	3.9	394	3.8	448	4.3	530	4.7	419	3.6
OK	141	1.4	96	0.9	113	1.1	115	1.1	80	0.8	110	1.0	110	0.9
OR	153	1.5	155	1.4	142	1.4	149	1.4	128	1.2	103	0.9	153	1.3
PA	693	6.9	767	7.1	624	6.0	478	4.6	660	6.4	539	4.8	658	5.6
RI	35	0.3	37	0.3	20	0.2	21	0.2	21	0.2	47	0.4	37	0.3
SC	237	2.4	186	1.7	218	2.1	173	1.7	155	1.5	131	1.2	179	1.5
SD	60	0.6	47	0.4	53	0.5	58	0.6	32	0.3	35	0.3	52	0.4
TN	329	3.3	291	2.7	265	2.6	238	2.3	198	1.9	202	1.8	164	1.4
TX	463	4.6	724	6.7	504	4.9	585	5.6	530	5.1	571	5.1	624	5.3
UT	58	0.6	37	0.3	81	0.8	58	0.6	45	0.4	83	0.7	110	0.9
VA	223	2.2	295	2.7	236	2.3	275	2.7	262	2.5	275	2.4	301	2.6
VT	20	0.2	18	0.2	24	0.2	25	0.2	25	0.2	23	0.2	32	0.3
WA	258	2.6	238	2.2	257	2.5	227	2.2	238	2.3	323	2.9	301	2.6
WI	283	2.8	294	2.7	243	2.4	245	2.4	168	1.6	243	2.2	234	2.0
WV	124	1.2	131	1.2	87	0.8	72	0.7	76	0.7	81	0.7	73	0.6
WY	10	<0.1	33	0.3	28	0.3	30	0.3	74	0.7	32	0.3	24	0.2
Other†	359	3.6	551	5.1	518	5.0	641	6.2	602	5.8	677	6.0	1,104	9.4
Total	**10,004**	**100.0**	**10,821**	**100.0**	**10,327**	**100.0**	**10,355**	**100.0**	**10,301**	**100.0**	**11,238**	**100.0**	**11,711**	**100.0**

* Number of reports per million of population. The population-based reporting rates were calculated by using the 11-year (1991–2001) average number of reports in each state as numerator and the average of 1990 and 2000 Bureau of the Census data for each state as denominator.
† Data include reports of foreign and unidentifiable origin.

TABLE 2 (*Continued*). Vaccine Adverse Event Reporting System (VAERS) reports and population-based reporting rates in the 50 states — United States, 1991–2001

State	1998		1999		2000		2001		All		Average
	No.	%	No.	%	No.	%	No.	%	No.	%	rate*
AK	90	0.8	58	0.4	95	0.6	107	0.7	733	0.6	113.2
AL	81	0.7	112	0.9	136	0.9	109	0.7	1,294	1.0	27.7
AR	103	0.9	105	0.8	133	0.9	87	0.6	1,329	1.0	48.1
AZ	141	1.3	194	1.5	190	1.3	176	1.2	1,579	1.2	32.6
CA	696	6.4	1,105	8.4	1,234	8.1	1,099	7.4	9,939	7.7	28.4
CO	201	1.8	238	1.8	214	1.4	206	1.4	2,201	1.7	52.7
CT	130	1.2	175	1.3	230	1.5	141	1.0	1,523	1.2	41.4
DC	30	0.3	40	0.3	43	0.3	54	0.4	400	0.3	61.7
DE	26	0.2	136	1.0	122	0.8	53	0.4	530	0.4	66.5
FL	475	4.4	523	4.0	511	3.4	510	3.5	4,820	3.7	30.3
GA	281	2.6	401	3.0	461	3.0	427	2.9	3,951	3.1	49.0
HI	38	0.3	70	0.5	60	0.4	62	0.4	556	0.4	43.6
IA	111	1.0	130	1.0	140	0.9	112	0.8	1,405	1.1	44.8
ID	87	0.8	85	0.6	85	0.6	113	0.8	1,030	0.8	81.4
IL	329	3.0	449	3.4	508	3.4	457	3.1	4,428	3.4	33.8
IN	176	1.6	232	1.8	282	1.9	263	1.8	2,140	1.7	33.5
KS	104	1.0	127	1.0	144	1.0	139	0.9	1,333	1.0	46.9
KY	96	0.9	144	1.1	171	1.1	198	1.3	1,270	1.0	29.9
LA	96	0.9	119	0.9	125	0.8	114	0.8	1,355	1.1	28.4
MA	302	2.8	427	3.2	367	2.4	379	2.6	3,513	2.7	51.7
MD	200	1.8	314	2.4	300	2.0	258	1.7	2,770	2.2	50.0
ME	50	0.5	92	0.7	78	0.5	118	0.8	822	0.6	59.7
MI	391	3.6	497	3.8	545	3.6	519	3.5	4,818	3.7	45.5
MN	216	2.0	279	2.1	256	1.7	252	1.7	2,539	2.0	49.7
MO	238	2.2	239	1.8	300	2.0	221	1.5	2,588	2.0	43.9
MS	79	0.7	96	0.7	110	0.7	96	0.7	1,058	0.8	35.5
MT	73	0.7	53	0.4	78	0.5	54	0.4	560	0.4	59.8
NC	280	2.6	313	2.4	324	2.1	316	2.1	3,262	2.5	40.4
ND	36	0.3	57	0.4	56	0.4	41	0.3	465	0.4	66.0
NE	86	0.8	91	0.7	84	0.6	82	0.6	843	0.7	46.6
NH	62	0.6	94	0.7	92	0.6	110	0.7	962	0.7	74.6
NJ	287	2.6	400	3.0	559	3.7	400	2.7	3,878	3.0	43.7
NM	60	0.6	76	0.6	95	0.6	95	0.6	779	0.6	42.5
NV	47	0.4	58	0.4	70	0.5	77	0.5	619	0.5	35.2
NY	554	5.1	771	5.9	887	5.9	679	4.6	7,269	5.6	35.8
OH	392	3.6	499	3.8	540	3.6	496	3.4	4,810	3.7	39.4
OK	123	1.1	129	1.0	145	1.0	116	0.8	1,278	1.0	35.2
OR	131	1.2	178	1.4	197	1.3	178	1.2	1,667	1.3	48.4
PA	538	4.9	722	5.5	869	5.7	667	4.5	7,215	5.6	54.3
RI	78	0.7	52	0.4	53	0.3	58	0.4	459	0.4	40.7
SC	161	1.5	228	1.7	243	1.6	177	1.2	2,088	1.6	50.6
SD	20	0.2	50	0.4	28	0.2	45	0.3	480	0.4	60.2
TN	139	1.3	194	1.5	173	1.1	196	1.3	2,389	1.9	41.1
TX	463	4.2	692	5.3	738	4.9	775	5.3	6,669	5.2	32.0
UT	74	0.7	116	0.9	121	0.8	120	0.8	903	0.7	41.5
VA	257	2.4	305	2.3	344	2.3	353	2.4	3,126	2.4	42.8
VA	257	2.4	305	2.3	344	2.3	353	2.4	3,126	2.4	42.8
VT	24	0.2	22	0.2	46	0.3	44	0.3	303	0.2	47.0
WA	270	2.5	317	2.4	367	2.4	299	2.0	3,095	2.4	52.3
WI	223	2.0	283	2.2	302	2.0	301	2.0	2,819	2.2	50.0
WV	73	0.7	71	0.5	86	0.6	81	0.5	955	0.7	48.2
WY	40	0.4	38	0.3	64	0.4	19	0.1	392	0.3	75.2
Other†	1,640	15.0	961	7.3	1,752	11.6	2,703	18.3	11,508	8.9	
Total	**10,898**	**100.0**	**13,157**	**100.0**	**15,153**	**100.0**	**14,752**	**100.0**	**128,717**	**100.0**	**44.1**

* Number of reports per million of population. The population-based reporting rates were calculated by using the 11-year (1991–2001) average number of reports in each state as numerator and the average of 1990 and 2000 Bureau of the Census data for each state as denominator.
† Data include reports of foreign and unidentifiable origin.

TABLE 3. Vaccine Adverse Event Reporting System (VAERS) reports and dose-based reporting rates for frequently reported vaccine types* — United States, 1991–2001

Vaccine type†	Year report received											
	1991		1992		1993		1994		1995		1996	
	No.	(%)§	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
ANTH	—**	0	—	0	4	(<.1)	—	0	—	0	—	0
DT	118	(1.2)	178	(1.6)	179	(1.7)	183	(1.8)	166	(1.6)	150	(1.3)
DTAP††	—	0	67	(0.6)	183	(1.8)	324	(3.1)	394	(3.8)	531	(4.7)
DTP	4,255	(42.6)	4,003	(37.0)	3,312	(32.1)	2,826	(27.3)	2,033	(19.8)	1,192	(10.6)
DTPH	—	0	—	0	176	(1.7)	952	(9.2)	1,422	(13.8)	1,783	(15.9)
FLU	537	(5.4)	875	(8.1)	1,159	(11.2)	1,549	(15.0)	1,228	(12.0)	1,403	(12.5)
HBHEPB	—	0	—	0	—	0	—	0	—	0	—	0
HEP	2,548	(25.5)	3,534	(32.7)	3,762	(36.5)	3,345	(32.4)	2,979	(29.0)	2,930	(26.2)
HEPA	—	0	—	0	—	0	—	0	95	(0.9)	278	(2.5)
HIBV§§	2,814	(28.2)	3,190	(29.5)	2,746	(26.6)	2,323	(22.5)	1,849	(18.0)	1,158	(10.3)
IPV	30	(0.3)	54	(0.5)	72	(0.7)	64	(0.6)	71	(0.7)	98	(0.9)
JEV	—	0	—	0	13	(0.1)	25	(0.2)	26	(0.3)	18	(0.2)
LYME	—	0	—	0	—	0	—	0	—	0	—	0
M	51	(0.5)	98	(0.9)	47	(0.5)	35	(0.3)	22	(0.2)	21	(0.2)
MEN	4	(<.1)	11	(0.1)	30	(0.3)	25	(0.2)	20	(0.2)	16	(0.1)
MMR	2,093	(20.9)	2,067	(19.1)	1,743	(16.9)	1,965	(19.0)	1,998	(19.4)	1,951	(17.4)
OPV	3,222	(32.2)	3,302	(30.5)	2,939	(28.5)	3,356	(32.5)	3,056	(29.7)	2,620	(23.4)
PNC	—	0	—	0	—	0	—	0	—	0	—	0
PPV	207	(2.1)	221	(2.0)	237	(2.3)	342	(3.3)	553	(5.4)	465	(4.2)
R	85	(0.9)	76	(0.7)	61	(0.6)	42	(0.4)	59	(0.6)	56	(0.5)
RAB	48	(0.5)	89	(0.8)	204	(2.0)	177	(1.7)	161	(1.6)	130	(1.2)
RV	—	0	—	0	—	0	—	0	—	0	—	0
TD	479	(4.8)	501	(4.6)	715	(6.9)	730	(7.1)	1,011	(9.8)	1,083	(9.7)
TTOX	64	(0.6)	73	(0.7)	82	(0.8)	93	(0.9)	145	(1.4)	141	(1.3)
TYP	99	(1.0)	129	(1.2)	99	(1.0)	176	(1.7)	116	(1.1)	162	(1.4)
VARCEL	—	0	—	0	—	0	—	0	649	(6.3)	1,904	(17.0)
YF	13	(0.1)	27	(0.2)	69	(0.7)	43	(0.4)	40	(0.4)	62	(0.6)
Other¶¶	53	(0.5)	58	(0.5)	35	(0.3)	37	(0.4)	62	(0.6)	50	(0.4)
Total***	**10,004**	†††	**10,821**	†††	**10,327**	†††	**10,355**	†††	**10,301**	†††	**11,238**	†††

* The frequently reported vaccine types were defined as the vaccine types for which a total of ≥100 reports were received during 1991–2001.

† VAERS coding terms for vaccine types. See the Vaccine Codes Used in This Report section for a description of each coding term. Each vaccine type might represent similar vaccines from multiple vaccine manufacturers. Vaccines were either reported alone or in combination with other vaccines.

§ Percentages represent the proportion of reports concerning the vaccine type among the total number of reports in each year.

¶ Number of reports per 100,000 net vaccine doses distributed. The dose-based reporting rates were calculated using the 11-year (1991–2001) total number of reports as numerators and the 11-year total number of net doses of vaccines distributed (Table 1) as denominators.

** Not available.

†† The dose-based reporting rate for DTAP was calculated using the sum of the total numbers of net distributed doses of DTAP and DTaP-HIB (Table 1) as denominator.

§§ The dose-based reporting rate for HIBV was calculated using the sum of the total numbers of net distributed doses of HIBV and DTaP-HIB (Table 1) as denominator.

¶¶ Data from vaccine types not listed in Table 3.

*** Total number of reports received in VAERS, by year, not the total of each column. The total percentages are not applicable because each report might include multiple vaccine types or vaccine combinations.

††† Not applicable.

TABLE 3 (*Continued*). Vaccine Adverse Event Reporting System (VAERS) reports and dose-based reporting rates for frequently reported vaccine types* — United States, 1991–2001

Vaccine type	Year report received: 1997 No.	1997 (%)	1998 No.	1998 (%)	1999 No.	1999 (%)	2000 No.	2000 (%)	2001 No.	2001 (%)	1991–2001 No.	1991–2001 Rate¶
ANTH	—	0	62	(0.6)	629	(4.8)	1,004	(6.7)	123	(0.8)	1,822	91.8
DT	173	(1.5)	82	(0.8)	79	(0.6)	135	(0.9)	131	(0.9)	1,574	14.9
DTAP††	1,175	(10.0)	1,772	(16.3)	2,515	(19.2)	2,996	(19.9)	4,059	(27.5)	14,016	12.5
DTP	675	(5.8)	312	(2.9)	293	(2.2)	203	(1.3)	187	(1.3)	19,291	26.2
DTPH	1,124	(9.6)	278	(2.6)	124	(0.9)	75	(0.5)	34	(0.2)	5,968	12.4
FLU	1,770	(15.1)	1,900	(17.5)	1,786	(13.6)	1,771	(11.8)	1,674	(11.3)	15,652	3.1
HBHEPB	31	(0.3)	128	(1.2)	300	(2.3)	621	(4.1)	940	(6.4)	2,020	12.9
HEP	2,966	(25.4)	2,802	(25.8)	2,755	(21.1)	2,604	(17.3)	2,334	(15.8)	32,559	11.8
HEPA	309	(2.6)	306	(2.8)	399	(3.0)	594	(3.9)	753	(5.1)	2,734	8.6
HIBV§§	1,178	(10.1)	1,378	(12.7)	1,842	(14.1)	1,783	(11.8)	1,884	(12.8)	22,145	18.1
IPV	365	(3.1)	642	(5.9)	1,169	(8.9)	2,220	(14.7)	3,135	(21.3)	7,920	13.1
JEV	30	(0.3)	33	(0.3)	25	(0.2)	31	(0.2)	28	(0.2)	229	19.1
LYME	—	0	—	0	386	(2.9)	781	(5.2)	367	(2.5)	1,534	103.1
M	26	(0.2)	33	(0.3)	28	(0.2)	11	(<0.1)	15	(0.1)	387	12.0
MEN	35	(0.3)	96	(0.9)	64	(0.5)	171	(1.1)	158	(1.1)	630	7.9
MMR	1,994	(17.0)	1,923	(17.7)	2,189	(16.7)	2,549	(16.9)	3,315	(22.5)	23,787	16.3
OPV	1,803	(15.4)	1,153	(10.6)	1,168	(8.9)	348	(2.3)	174	(1.2)	23,141	15.1
PNC	—	0	—	0	—	0	817	(5.4)	2,871	(19.5)	3,688	12.8
PPV	590	(5.0)	809	(7.4)	958	(7.3)	958	(6.4)	1,058	(7.2)	6,398	10.9
R	46	(0.4)	47	(0.4)	24	(0.2)	74	(0.5)	41	(0.3)	611	18.8
RAB	198	(1.7)	112	(1.0)	126	(1.0)	190	(1.3)	126	(0.9)	1,561	68.3
RV	—	0	24	(0.2)	540	(4.1)	117	(0.8)	27	(0.2)	708	156.3
TD	1,001	(8.6)	1,079	(9.9)	1,160	(8.9)	1,207	(8.0)	726	(4.9)	9,692	6.3
TTOX	123	(1.1)	126	(1.2)	134	(1.0)	130	(0.9)	119	(0.8)	1,230	4.9
TYP	141	(1.2)	136	(1.3)	157	(1.2)	220	(1.5)	217	(1.5)	1,652	37.8
VARCEL	2,424	(20.7)	1,929	(17.7)	2,708	(20.7)	2,870	(19.1)	2,696	(18.3)	15,180	50.0
YF	42	(0.4)	53	(0.5)	69	(0.5)	93	(0.6)	104	(0.7)	615	9.6
Other¶¶	33	(0.3)	34	(0.3)	53	(0.4)	137	(0.9)	438	(3.0)	—	—
Total***	**11,711**	†††	**10,898**	†††	**13,157**	†††	**15,153**	†††	**14,752**	†††	**128,717**	†††

* The frequently reported vaccine types were defined as the vaccine types for which a total of ≥100 reports were received during 1991–2001.
† VAERS coding terms for vaccine types. See the Vaccine Codes Used in This Report section for a description of each coding term. Each vaccine type might represent similar vaccines from multiple vaccine manufacturers. Vaccines were either reported alone or in combination with other vaccines.
§ Percentages represent the proportion of reports concerning the vaccine type among the total number of reports in each year.
¶ Number of reports per 100,000 net vaccine doses distributed. The dose-based reporting rates were calculated using the 11-year (1991–2001) total number of reports as numerators and the 11-year total number of net doses of vaccines distributed (Table 1) as denominators.
** Not available.
†† The dose-based reporting rate for DTAP was calculated using the sum of the total numbers of net distributed doses of DTAP and DTaP-HIB (Table 1) as denominator.
§§ The dose-based reporting rate for HIBV was calculated using the sum of the total numbers of net distributed doses of HIBV and DTaP-HIB (Table 1) as denominator.
¶¶ Data from vaccine types not listed in Table 3.
*** Total number of reports received in VAERS, by year, not the total of each column. The total percentages are not applicable because each report might include multiple vaccine types or vaccine combinations.
††† Not applicable.

TABLE 4. Vaccine Adverse Event Reports System reports, by age groups — United States, 1991–2001

Year	Age groups (yrs): <1 No.	<1 (%)	1–6 No.	1–6 (%)	7–17 No.	7–17 (%)	18–64 No.	18–64 (%)	≥65 No.	≥65 (%)	Unknown* No.	Unknown* (%)	Year total No.	Year total (%)
1991	2,543	(25.4)	2,531	(25.3)	394	(3.9)	2,936	(29.3)	281	(2.8)	1,319	(13.2)	**10,004**	**(100.0)**
1992	2,426	(22.4)	2,378	(22.0)	458	(4.2)	3,744	(34.6)	416	(3.8)	1,399	(12.9)	**10,821**	**(100.0)**
1993	2,296	(22.2)	2,154	(20.9)	537	(5.2)	3,838	(37.2)	410	(4.0)	1,092	(10.6)	**10,327**	**(100.0)**
1994	2,616	(25.3)	2,208	(21.3)	547	(5.3)	3,411	(32.9)	472	(4.6)	1,101	(10.6)	**10,355**	**(100.0)**
1995	2,439	(23.7)	2,484	(24.1)	700	(6.8)	3,204	(31.1)	503	(4.9)	971	(9.4)	**10,301**	**(100.0)**
1996	2,159	(19.2)	2,832	(25.2)	943	(8.4)	3,629	(32.3)	511	(4.5)	1,164	(10.4)	**11,238**	**(100.0)**
1997	1,732	(14.8)	3,294	(28.1)	1,240	(10.6)	3,734	(31.9)	698	(6.0)	1,013	(8.6)	**11,711**	**(100.0)**
1998	1,356	(12.4)	2,891	(26.5)	1,317	(12.1)	3,670	(33.7)	706	(6.5)	958	(8.8)	**10,898**	**(100.0)**
1999	1,743	(13.2)	3,557	(27.0)	1,496	(11.4)	4,563	(34.7)	710	(5.4)	1,088	(8.3)	**13,157**	**(100.0)**
2000	1,725	(11.4)	4,466	(29.5)	1,443	(9.5)	5,384	(35.5)	818	(5.4)	1,317	(8.7)	**15,153**	**(100.0)**
2001	2,260	(15.3)	5,620	(38.1)	1,170	(7.9)	3,913	(26.5)	774	(5.2)	1,015	(6.9)	**14,752**	**(100.0)**
Total	**23,295**	**(18.1)**	**34,415**	**(26.7)**	**10,245**	**(8.0)**	**42,026**	**(32.6)**	**6,299**	**(4.9)**	**12,437**	**(9.7)**	**128,717**	**(100.0)**

*Age unknown because of missing information regarding date of birth and age.

TABLE 5. Vaccine Adverse Event Reporting System (VAERS) reports of frequently reported vaccines or vaccine combinations* — United States, 1991–1995

Vaccines or vaccine combinations	No.	(%†)	Total %
HEP	12,519	(24.2)	24.2
DTP HIBV OPV	5,344	(10.3)	34.5
FLU	4,696	(9.1)	43.5
MMR	3,386	(6.5)	50.1
TD	2,510	(4.8)	54.9
DTP OPV	2,300	(4.4)	59.4
DTP	1,595	(3.1)	62.4
DTP HIBV	1,564	(3.0)	65.5
DTP HEP HIBV OPV	1,543	(3.0)	68.4
DTP MMR OPV	1,523	(2.9)	71.4
DTP HIBV MMR OPV	1,429	(2.8)	74.1
PPV	974	(1.9)	76.0
HIBV MMR	880	(1.7)	77.7
DTPH OPV	877	(1.7)	79.4
DTPH HEP OPV	784	(1.5)	80.9
HIBV	722	(1.4)	82.3
RAB	646	(1.2)	83.6
VARCEL	574	(1.1)	84.7
FLU PPV	455	(0.9)	85.5
TYP	408	(0.8)	86.3
DT	397	(0.8)	87.1
MMR TD	395	(0.8)	87.9
TTOX	384	(0.7)	88.6
DTPH	375	(0.7)	89.3
R	306	(0.6)	89.9
DTAP MMR OPV	265	(0.5)	90.4
DTAP OPV	227	(0.4)	90.9
DTP HIBV MMR	218	(0.4)	91.3
DTP HEP HIBV	215	(0.4)	91.7
M	197	(0.4)	92.1
DTP MMR	178	(0.3)	92.4
DTPH MMR OPV	156	(0.3)	92.7
DTAP HIBV MMR OPV	152	(0.3)	93.0
DTPH MMR	141	(0.3)	93.3
HEP MMR	128	(0.2)	93.5
HIBV MMR OPV	120	(0.2)	93.8
DTAP	117	(0.2)	94.0
MMR OPV TD	101	(0.2)	94.2
DTP HEP OPV	100	(0.2)	94.4
DTPH HEP	92	(0.2)	94.6
DTP HEP HIBV MMR OPV	89	(0.2)	94.7
HIBV OPV	89	(0.2)	94.9
MMR OPV	80	(0.2)	95.1
HEP TD	72	(0.1)	95.2
DT OPV	68	(0.1)	95.3
DT MMR OPV	67	(0.1)	95.5
DT MMR	66	(0.1)	95.6
FLU TD	63	(0.1)	95.7
MR	63	(0.1)	95.8
OPV	63	(0.1)	96.0
HEPA	61	(0.1)	96.1
YF	58	(0.1)	96.2
HEP HIBV OPV	57	(0.1)	96.3
DTP HIBV IPV	52	(0.1)	96.4
OPV TD	52	(0.1)	96.5
TD YF	50	(<0.1)	96.6
Other§	1,765	(3.4)	100.0

* The frequently reported vaccines or vaccine combinations were defined as the vaccines or vaccine combinations for which ≥50 reports were received during1991–1995.
† Percentage represents the proportion of reports that include the vaccine or vaccine combinations among the total number of reports (51,808) during 1991–1995.
§ Data from other vaccines or vaccine combinations not listed in Table 5.

TABLE 6. Vaccine Adverse Event Reporting System reports of frequently reported vaccines or vaccine combinations* — United States, 1996–2001

Vaccines or vaccine combinations	No.	(%†)	Total %
VARCEL	9,820	(12.8)	12.8
HEP	9,022	(11.7)	24.5
FLU	8,125	(10.6)	35.1
TD	4,053	(5.3)	40.3
MMR	3,644	(4.7)	45.1
PPV	2,857	(3.7)	48.8
ANTH	1,635	(2.1)	50.9
FLU PPV	1,513	(2.0)	52.9
LYME	1,505	(2.0)	54.8
DTAP	1,242	(1.6)	56.5
HEPA	1,141	(1.5)	57.9
MMR VARCEL	1,117	(1.5)	59.4
DTAP HIBV IPV	1,109	(1.4)	60.8
PNC	1,014	(1.3)	62.1
DTPH HEP OPV	972	(1.3)	63.4
DTPH OPV	901	(1.2)	64.6
DTAP MMR OPV	851	(1.1)	65.7
DTAP IPV MMR	840	(1.1)	66.8
RAB	753	(1.0)	67.8
DTAP HIBV	711	(0.9)	68.7
DTAP HEP HIBV IPV	622	(0.8)	69.5
DTAP HBHEPB IPV	583	(0.8)	70.3
TTOX	547	(0.7)	71.0
HEP TD	520	(0.7)	71.6
HEP MMR	495	(0.6)	72.3
DTP HIBV OPV	460	(0.6)	72.9
DTPH	440	(0.6)	73.5
DTP HEP HIBV OPV	438	(0.6)	74.0
DTAP HBHEPB IPV PNC	437	(0.6)	74.6
DTAP PV	424	(0.6)	75.1
MMR TD	404	(0.5)	75.7
HIBV MMR	399	(0.5)	76.2
TYP	388	(0.5)	76.7
DTAP HIBV IPV PNC	374	(0.5)	77.2
HIBV	361	(0.5)	77.6
DTAP HIBV OPV	332	(0.4)	78.1
DTAP HIBV MMR	314	(0.4)	78.5
DTAP OPV	314	(0.4)	78.9
DTPH MMR	312	(0.4)	79.3
HEP VARCEL	280	(0.4)	79.7
R	265	(0.3)	80.0
DT	258	(0.3)	80.3
DTP	255	(0.3)	80.7
HEP HEPA	244	(0.3)	81.0
DTAP MMR	234	(0.3)	81.3
DTP HIBV	232	(0.3)	81.6
MEN	211	(0.3)	81.9
HIBV MMR VARCEL	203	(0.3)	82.1
DTAP HEP HIBV	194	(0.3)	82.4
HEP MMR TD	185	(0.2)	82.6
RV	180	(0.2)	82.9
DTAP HIBV MMR OPV	179	(0.2)	83.1
DTAP HIBV IPV RV	176	(0.2)	83.3
DTAP HIBV MMR VARCEL	176	(0.2)	83.6
DTAP HEP HIBV OPV	174	(0.2)	83.8
DTP MMR OPV	173	(0.2)	84.0
DTP OPV	167	(0.2)	84.2
DTAP HEP MMR OPV	163	(0.2)	84.4
DTAP VARCEL	162	(0.2)	84.6
DTAP HIBV PNC	158	(0.2)	84.9
DTPH MMR OPV	158	(0.2)	85.1
MMR PNC VARCEL	146	(0.2)	85.2
FLU TD	144	(0.2)	85.4

TABLE 6 (*Continued*). Vaccine Adverse Event Reporting System reports of frequently reported vaccines or vaccine combinations* — United States, 1996–2001

Vaccines or vaccine combinations	No.	(%†)	Total %
DTAP HIBV IPV MMR	142	(0.2)	85.6
DTAP HEP	140	(0.2)	85.8
DTP HIBV MMR	138	(0.2)	86.0
DTAP IPV MMR VARCEL	137	(0.2)	86.2
DTAP PNC	135	(0.2)	86.3
DTAP MMR OPV VARCEL	131	(0.2)	86.5
HEPA TYP	129	(0.2)	86.7
PPV TD	116	(0.2)	86.8
YF	112	(0.1)	87.0
DTPH HEP	110	(0.1)	87.1
DTAP IPV PNC	109	(0.1)	87.3
DTP HIBV IPV	108	(0.1)	87.4
M	108	(0.1)	87.5
MMR OPV VARCEL	108	(0.1)	87.7
DTAP HBHEPB	107	(0.1)	87.8
IPV MMR VARCEL	106	(0.1)	88.0
DTAP HIBV IPV MMR VARCEL	104	(0.1)	88.1
IPV	104	(0.1)	88.2
DTAP HEP OPV	99	(0.1)	88.3
DTAP HIBV MMR OPV VARCEL	99	(0.1)	88.5
DTPH HEP IPV	99	(0.1)	88.6
DTPH IPV	98	(0.1)	88.7
DTAP HEP HIBV IPV PNC	97	(0.1)	88.9
HBHEPB	93	(0.1)	89.0
JEV	88	(0.1)	89.1
HEP PNC	86	(0.1)	89.2
DTAP HEPA IPV MMR	85	(0.1)	89.3
DTAP OPV VARCEL	85	(0.1)	89.4
DTAP HEP HIBV IPV RV	80	(0.1)	89.5
MMR OPV	78	(0.1)	89.6
UNK	78	(0.1)	89.7
DTPH MMR VARCEL	77	(0.1)	89.8
HEP MMR VARCEL	77	(0.1)	89.9
PNC VARCEL	76	(<0.1)	90.0
FLU PPV TD	74	(<0.1)	90.1
HEPA TD	74	(<0.1)	90.2
DTPH HEP MMR OPV	73	(<0.1)	90.3
DTAP HIBV VARCEL	71	(<0.1)	90.4
DTP HIBV MMR OPV	68	(<0.1)	90.5
OPV	68	(<0.1)	90.6
DTAP HBHEPB PNC	66	(<0.1)	90.7
DTP MMR	66	(<0.1)	90.8
DT HEP	64	(<0.1)	90.8
DTAP HBHEPB IPV RV	64	(<0.1)	90.9
DTAP HEP HIBV PNC	64	(<0.1)	91.0
DTAP MMR VARCEL	64	(<0.1)	91.1
IPV MMR	64	(<0.1)	91.2
DTAP HBHEPB IPV MMR	61	(<0.1)	91.3
DTAP HEP IPV	59	(<0.1)	91.3
HIBV VARCEL	59	(<0.1)	91.4
DTP HEP HIBV IPV	58	(<0.1)	91.5
DTP HEP OPV	56	(<0.1)	91.6
MMR PNC	55	(<0.1)	91.6
FLU HEP	54	(<0.1)	91.7
HEPA PNC	52	(<0.1)	91.8
DTAP HEP IPV MMR	50	(<0.1)	91.8
Other§	6,280	(8.2)	100.0

* Frequently reported vaccines or vaccine combinations were defined as the vaccines or vaccine combinations for which ≥50 reports were received during1996–2001.

† Percentage represents the proportion of reports that include the vaccine or vaccine combinations among the total number of reports (76,909) during1996–2001.

§ Data from other vaccines or vaccine combinations not listed in Table 6.

TABLE 7. Frequently reported adverse events* in the Vaccine Adverse Event Reporting System (VAERS) — United States, 1991–2001

Adverse event	No.	(%)	Adverse event	No.	(%)	Adverse event	No.	(%)
Fever	33,172	(25.8)	Abdominal pain	2,254	(1.8)	Facial paralysis	580	(0.5)
Injection-site hypersensitivity	20,359	(15.8)	Cellulitis	2,148	(1.7)	Confusion	579	(0.4)
Rash	14,112	(11.0)	Lab test abnormal	2,056	(1.6)	Paralysis	574	(0.4)
Injection-site edema	13,960	(10.8)	Myasthenia	1,812	(1.4)	Injection-site inflammation	572	(0.4)
Vasodilatation	13,929	(10.8)	Cyanosis	1,804	(1.4)	Hypoxia	566	(0.4)
Injection-site pain	10,382	(8.1)	Chest pain	1,752	(1.4)	Joint disorder	562	(0.4)
Infection	9,741	(7.6)	Reaction unevaluable	1,704	(1.3)	Respiratory disorder	556	(0.4)
Agitation	9,443	(7.3)	Apnea	1,618	(1.3)	Ataxia	555	(0.4)
Pruritus	8,908	(6.9)	Exacerbation of underlying condition	1,606	(1.2)	Eye disorder	543	(0.4)
Pain	8,755	(6.8)	Otitis media	1,538	(1.2)	Hyperventilation	539	(0.4)
Myalgia	8,233	(6.4)	Insomnia	1,526	(1.2)	Autism	530	(0.4)
Urticaria	7,793	(6.1)	Twitching	1,511	(1.2)	Sedimentation rate increased	530	(0.4)
Possible vaccine failure	7,625	(5.9)	Febrile seizure	1,490	(1.2)	Accidental injury	530	(0.4)
Headache	7,068	(5.5)	Asthma	1,373	(1.1)	Petechiae	510	(0.4)
Injection-site mass	6,987	(5.4)	Ecchymosis	1,347	(1.0)	Amblyopia	507	(0.4)
Vomiting	6,633	(5.2)	Neck pain	1,323	(1.0)	Mental retardation	498	(0.4)
Asthenia	6,431	(5.0)	Positive rechallenge	1,292	(1.0)	Erythema multiforme	483	(0.4)
Convulsion	5,639	(4.4)	Back pain	1,277	(1.0)	Anemia	482	(0.4)
Maculopapular rash	5,489	(4.3)	Tachycardia	1,269	(1.0)	Encephalitis	480	(0.4)
Arthralgia	5,364	(4.2)	Eyes gaze upward	1,249	(1.0)	SGOT increased†	477	(0.4)
Nausea	5,260	(4.1)	Neuropathy	1,154	(0.9)	SGPT increased§	459	(0.4)
Vesiculobullous rash	5,237	(4.1)	Skin nodule	1,134	(0.9)	Thinking abnormality	457	(0.4)
Screaming syndrome	5,020	(3.9)	Arthrosis	1,129	(0.9)	Dyspepsia	454	(0.4)
Dizziness	4,274	(3.3)	Hypertension	1,038	(0.8)	Anaphylactoid reaction	452	(0.4)
Peripheral edema	4,165	(3.2)	Hypotension	1,021	(0.8)	Gastrointestinal disorder	449	(0.3)
Malaise	4,159	(3.2)	Leukocytosis	1,021	(0.8)	Previous reaction	442	(0.3)
Somnolence	4,093	(3.2)	Abnormal gait	998	(0.8)	Serum sickness	428	(0.3)
Paresthesia	4,075	(3.2)	Arthritis	972	(0.8)	Injection-site abscess	426	(0.3)
Crying abnormal	4,017	(3.1)	Skin discoloration	909	(0.7)	Abnormal electroencephalogram	420	(0.3)
Diarrhea	3,854	(3.0)	Herpes zoster	892	(0.7)	Leukopenia	417	(0.3)
Dyspnea	3,692	(2.9)	Laryngismus	881	(0.7)	Sepsis	416	(0.3)
Pharyngitis	3,623	(2.8)	Pneumonia	879	(0.7)	Weight loss	415	(0.3)
Hypokinesia	3,536	(2.7)	Conjunctivitis	860	(0.7)	Vertigo	412	(0.3)
Edema	3,504	(2.7)	Speech disorder	848	(0.7)	Heart arrest	410	(0.3)
Chills	3,403	(2.6)	Neck rigidity	829	(0.6)	Bronchitis	407	(0.3)
Stupor	3,272	(2.5)	Guillain-Barré syndrome	820	(0.6)	Grand malconvulsion	402	(0.3)
Anorexia	3,219	(2.5)	Nausea and vomiting	812	(0.6)	Anxiety	391	(0.3)
Pallor	3,094	(2.4)	Sudden infant death	808	(0.6)	Hepatitis	387	(0.3)
Face edema	2,869	(2.2)	Chills and fever	722	(0.6)	Skin disorder	364	(0.3)
Rhinitis	2,733	(2.1)	Liver function tests abnormal	717	(0.6)	Ear disorder	362	(0.3)
Cough increased	2,657	(2.1)	Personality disorder	678	(0.5)	Bradycardia	359	(0.3)
Lymphadenopathy	2,635	(2.0)	Thrombocytopenia	640	(0.5)	Infect viral	358	(0.3)
Hypotonia	2,619	(2.0)	Lung disorder	614	(0.5)	Vasculitis	353	(0.3)
Tremor	2,615	(2.0)	Abnormal vision	609	(0.5)	Hemorrhage	338	(0.3)
Hypertonia	2,545	(2.0)	Dehydration	603	(0.5)	Increased salivation	336	(0.3)
Flu syndrome	2,532	(2.0)	Dysphagia	603	0.5)	Lacrimation disorder	334	(0.3)
Injection-site reaction	2,496	(1.9)	Cerebrospinal fluid abnormal	600	(0.5)	Hypoventilation	321	(0.2)
Syncope	2,437	(1.9)	Meningitis	592	(0.5)	Abscess	318	(0.2)
Sweating	2,301	(1.8)	Skin ulcer	584	(0.5)	Jaundice	317	(0.2)
Allergic reaction	2,281	(1.8)	Nervousness	583	(0.5)	Eye pain	316	(0.2)

* Frequently reported adverse events were defined as the adverse events that were mentioned in ≥100 VAERS reports during1991–2001. Each report might include multiple adverse events. The percentages represent the proportion of each frequently reported adverse event among the total number of VAERS reports (128,717) during 1991–2001.
† SGOT — Serum glutamic oxaloacetic transaminase.
§ SGPT — Serum glutamic pyruvic transaminase.

TABLE 7 (*Continued*). Frequently reported adverse events* in the Vaccine Adverse Event Reporting System (VAERS) — United States, 1991–2001

Adverse event	No.	(%)	Adverse event	No.	(%)
Palpitations	313	(0.2)	Gastrointestinal hemorrhage	183	(0.1)
Tongue edema	310	(0.2)	Reflexes decreased	178	(0.1)
Ear pain	302	(0.2)	Opisthotonos	173	(0.1)
Sinusitis	298	(0.2)	Dry mouth	171	(0.1)
Angioedema	296	(0.2)	Optic neuritis	171	(0.1)
Rheumatoid arthritis	295	(0.2)	Thrombocythemia	171	(0.1)
Immune system disorder	292	(0.2)	Lactic dehydrogenase increased	167	(0.1)
Antinuclear antibody present	288	(0.2)	Arrhythmia	164	(0.1)
Deafness	287	(0.2)	Epistaxis	163	(0.1)
Myelitis	280	(0.2)	Lupus syndrome	163	(0.1)
Hypothermia	275	(0.2)	Photophobia	163	(0.1)
Hyperglycemia	268	(0.2)	Eczema	159	(0.1)
Tinnitus	268	(0.2)	Hallucinations	157	(0.1)
Migraine	267	(0.2)	Hematuria	156	(0.1)
Thrombocytopenic purpura	267	(0.2)	Tongue disorder	156	(0.1)
Multiple sclerosis	264	(0.2)	Neuralgia	155	(0.1)
Amnesia	262	(0.2)	Lung edema	152	(0.1)
Incoordination	261	(0.2)	Circumoral paresthesia	152	(0.1)
Alopecia	260	(0.2)	Diplopia	150	(0.1)
Voice alteration	259	(0.2)	Thirst	148	(0.1)
Abortion	257	(0.2)	Bone disorder	145	(0.1)
Shock	253	(0.2)	Intussusception	143	(0.1)
Purpura	251	(0.2)	Fetal disorder	142	(0.1)
Bacterial infection	250	(0.2)	Muscle atrophy	140	(0.1)
Skin striae	247	(0.2)	Mydriasis	139	(0.1)
Mouth ulceration	246	(0.2)	Emotional liability	138	(0.1)
Constipation	242	(0.2)	Blindness	137	(0.1)
Acute brain syndrome	240	(0.2)	Tendon disorder	137	(0.1)
Hypesthesia	238	(0.2)	Hostility	136	(0.1)
Urinary incontinence	237	(0.2)	Photosensitivity reaction	131	(0.1)
Movement disorder	237	(0.2)	Visual field defect	131	(0.1)
Coma	230	(0.2)	Apathy	129	(0.1)
Hyperkinesia	227	(0.2)	Hemiplegia	129	(0.1)
Staladenitis	226	(0.2)	Lymphocytosis	129	(0.1)
Cardiovascular disorder	225	(0.2)	Pustular rash	128	(<0.1)
Encephalopathy	224	(0.2)	Creatine phosphokinase increased	127	(<0.1)
Urine abnormality	223	(0.2)	Stomatitis	121	(<0.1)
Bilirubinemia	221	(0.2)	Injection-site hemorrhage	119	(<0.1)
Gastroenteritis	218	(0.2)	Intracranial hypertension	118	(<0.1)
Peripheral vascular disorder	215	(0.2)	Gamma glutamyl transpeptidase increased	117	(<0.1)
Urinary tract infection	213	(0.2)	Abnormal stools	111	(<0.1)
Exfoliative dermatitis	212	(0.2)	Hypochromic anemia	109	(<0.1)
Myopathy	199	(0.2)	Bone pain	109	(<0.1)
Alkaline phosphatase increased	199	(0.2)	Cerebrovascular accident	106	(<0.1)
Depression	196	(0.2)	Hepatomegaly	106	(<0.1)
Diabetes mellitus	196	(0.2)	Myositis	103	(<0.1)
Neuritis	195	(0.2)	Parotid gland enlargement	103	(<0.1)
Taste perversion	191	(0.1)	Flatulence	102	(<0.1)
Laryngitis	190	(0.1)	Liver damage	102	(<0.1)
Generalized spasm	186	(0.1)			

* Frequently reported adverse events were defined as the adverse events that were mentioned in ≥100 VAERS reports during1991–2001. Each report might include multiple adverse events. The percentages represent the proportion of each frequently reported adverse event among the total number of VAERS reports (128,717) during 1991–2001.

† SGOT — Serum glutamic oxaloacetic transaminase.

§ SGPT — Serum glutamic pyruvic transaminase.

TABLE 8. Vaccine Adverse Event Reporting System (VAERS) reports, by reporting source — United States, 1991–2001

	Year report received											
	1991		1992		1993		1994		1995		1996	
Reporting source	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Manufacturer	3,947	(39.5)	4,207	(38.9)	3,661	(35.5)	3,290	(31.8)	3,212	(31.2)	4,261	(37.9)
Patient/Parent	101	(1.0)	134	(1.2)	176	(1.7)	265	(2.6)	372	(3.6)	449	(4.0)
Provider	1,138	(11.4)	1,385	(12.8)	1,328	(12.9)	1,558	(15.0)	1,842	(17.9)	2,059	(18.3)
State health coordinator	3,992	(39.9)	3,974	(36.7)	3,984	(38.6)	4,019	(38.8)	3,566	(34.6)	2,998	(26.7)
Other*	486	(4.9)	665	(6.1)	726	(7.0)	697	(6.7)	765	(7.4)	822	(7.3)
Unknown†	340	(3.4)	456	(4.2)	452	(4.4)	526	(5.1)	544	(5.3)	649	(5.8)
Total	**10,004**	**(100.0)**	**10,821**	**(100.0)**	**10,327**	**(100.0)**	**10,355**	**(100.0)**	**10,301**	**(100.0)**	**11,238**	**(100.0)**

TABLE 8 (*Continued*). Vaccine Adverse Event Reporting System (VAERS) reports, by reporting source — United States, 1991–2001

	Year report received											
	1997		1998		1999		2000		2001		Total	
Reporting source	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Manufacturer	4,662	(39.8)	3,861	(35.4)	4,670	(35.5)	5,846	(38.6)	4,946	(33.5)	**46,563**	**(36.2)**
Patient/Parent	422	(3.6)	482	(4.4)	966	(7.3)	1,087	(7.2)	902	(6.1)	**5,356**	**(4.2)**
Provider	1,945	(16.6)	1,968	(18.1)	2,870	(21.8)	4,454	(29.4)	5,207	(35.3)	**25,754**	**(20.0)**
State health coordinator	3,244	(27.7)	2,927	(26.9)	2,531	(19.2)	2,178	(14.4)	2,115	(14.3)	**35,528**	**(27.6)**
Other*	832	(7.1)	960	(8.8)	1,378	(10.5)	1,102	(7.3)	997	(6.8)	**9,430**	**(7.3)**
Unknown†	606	(5.2)	700	(6.4)	742	(5.6)	486	(3.2)	585	(4.0)	**6,086**	**(4.7)**
Total	**11,711**	**(100.0)**	**10,898**	**(100.0)**	**13,157**	**(100.0)**	**15,153**	**(100.0)**	**14,752**	**(100.0)**	**128,717**	**(100.0)**

* Reported by persons other than manufacturers, patients/parents, providers, or state health coordinators.
† Unknown reporting source because of missing information.

TABLE 9. Nonserious and serious* Vaccine Adverse Event Report System (VAERS)† reports — United States, 1991–2001

	Year report received											
	1991		1992		1993		1994		1995		1996	
Category	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Nonserious total	8,703	(87.0)	9,380	(86.7)	8,875	(85.9)	8,810	(85.1)	8,835	(85.8)	9,783	(87.1)
Serious												
Patient died	167	(1.7)	228	(2.1)	235	(2.3)	236	(2.3)	159	(1.5)	152	(1.4)
Life-threatening illness	142	(1.4)	223	(2.1)	182	(1.8)	220	(2.1)	223	(2.2)	217	(1.9)
Required hospitalization	1,019	(10.2)	1,079	(10.0)	1,091	(10.6)	1,152	(11.1)	1,145	(11.1)	1,100	(9.8)
Resulted in prolongation of hospitalization	45	(0.4)	37	(0.3)	62	(0.6)	76	(0.7)	62	(0.6)	122	(1.1)
Resulted in permanent disability	172	(1.7)	151	(1.4)	182	(1.8)	243	(2.3)	189	(1.8)	227	(2.0)
Total	1,301	(13.0)	1,441	(13.3)	1,452	(14.1)	1,545	(14.9)	1,466	(14.2)	1,455	(12.9)
TOTAL§	**10,004**	**(100.0)**	**10,821**	**(100.0)**	**10,327**	**(100.0)**	**10,355**	**(100.0)**	**10,301**	**(100.0)**	**11,238**	**(100.0)**

TABLE 9 (*Continued*). Nonserious and serious* Vaccine Adverse Event Report System (VAERS)† reports — United States, 1991–2001

	Year report received											
	1997		1998		1999		2000		2001		Total	
Category	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Nonserious total	10,123	(86.4)	9,225	(84.6)	11,120	(84.5)	13,147	(86.8)	12,420	(84.2)	110,421	(85.8)
Serious												
Patient died	176	(1.5)	172	(1.6)	180	(1.4)	213	(1.4)	224	(1.5)		
Life-threatening illness	212	(1.8)	246	(2.3)	369	(2.8)	279	(1.8)	306	(2.1)		
Required hospitalization	1,205	(10.3)	1,209	(11.1)	1,424	(10.8)	1,373	(9.1)	1,527	(10.4)		
Resulted in prolongation of hospitalization	163	(1.4)	415	(3.8)	322	(2.4)	62	(0.4)	91	(0.6)		
Resulted in permanent disability	258	(2.2)	313	(2.9)	420	(3.2)	428	(2.8)	594	(4.0)		
Total	1,588	(13.6)	1,673	(15.4)	2,037	(15.5)	2,006	(13.2)	2,332	(15.8)	18,296	(14.2)
TOTAL§	**11,711**	**(100.0)**	**10,898**	**(100.0)**	**13,157**	**(100.0)**	**15,153**	**(100.0)**	**14,752**	**(100.0)**	**128,717**	**(100.0)**

* According to the regulatory definition, serious adverse events involve hospitalization or prolongation of hospitalization, death, or reported life-threatening illness or permanent disability. Food and Drug Administration 21 CFR Part 600.80. Postmarketing reporting of adverse experiences. Federal Register 1997;62:52252–3.
† Serious categories are not mutually exclusive. One VAERS report may involve >1 serious category. The percentages for each serious category represent the proportion of the number of reports involved in that category among the total number of reports in each year.
§ Total numbers of reports received in VAERS, by year (not the total of each column), which equal to the sum of the nonserious totals and the serious totals.

TABLE 10. Vaccine Adverse Event Report System (VAERS) reports on DTaP,* DTP,† and DTPH§ for children aged <7 years — United States, 1991–2001

Report year	Nonserious				Serious¶			
	DTAP	DTP	DTPH	Total	DTAP	DTP	DTPH	Total
1991	—**	3,579	—	**3,579**	—	662	—	**662**
1992	59	3,325	—	**3,384**	6	651	—	**657**
1993	160	2,717	135	**3,012**	20	570	41	**631**
1994	288	2,275	736	**3,299**	34	524	209	**767**
1995	349	1,650	1,173	**3,172**	42	355	247	**644**
1996	476	955	1,524	**2,955**	51	220	250	**521**
1997	973	496	918	**2,387**	194	157	203	**554**
1998	1,468	184	238	1,890	285	113	38	**436**
1999	2,003	177	86	**2,266**	490	107	35	**632**
2000	2,484	97	33	**2,614**	476	92	40	**608**
2001	3,432	94	17	**3,543**	576	80	15	**671**
Total	**11,692**	**15,549**	**4,860**	**32,101**	**2,174**	**3,531**	**1,078**	**6,783**
Rate††	10.5	21.1	10.1	**13.7**	1.9	4.8	2.2	**2.9**

* Diphtheria and tetanus toxoids and acellular pertussis vaccine.

† Diphtheria and tetanus toxoids and pertussis vaccine.

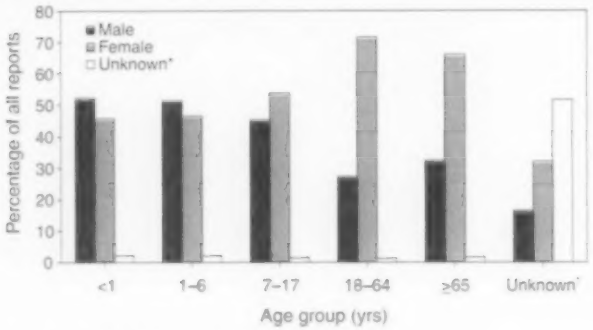
§ Diphtheria and tetanus toxoids and pertussis vaccine and *Haemophilus* b conjugate vaccine.

¶ According to the regulatory definition, serious adverse events involve hospitalization or prolongation of hospitalization, death, or reported life-threatening illness or permanent disability. Food and Drug Administration. 21 CFR Part 600.80. Postmarketing reporting of adverse experiences. Federal Register 1997:62:52252–3.

** Not available.

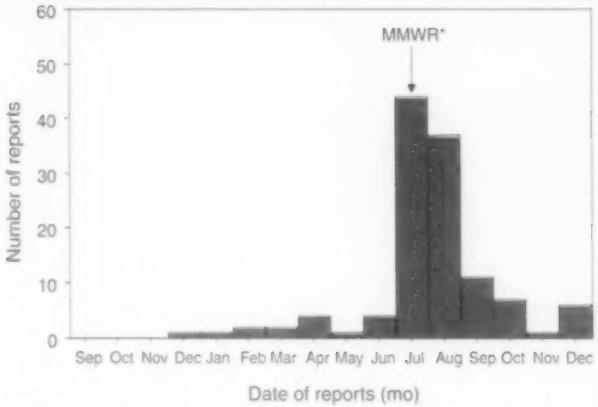
†† Number of reports per 100,000 net doses distributed. Calculated by using the total numbers of reports as numerators and the total net doses of the vaccines distributed (Table 1) as denominators.

FIGURE 1. Vaccine Adverse Event Reporting System (VAERS) reports, by age and sex — United States, 1991–2001



* Age not included because of missing information.
† Sex not included because of missing information.

FIGURE 2. Number of intussusception reports after the rhesus rotavirus vaccine-tetravalent (RRV-TV) — United States, September 1998–December 1999



* CDC. Intussusception among recipients of rotavirus vaccine—United States, 1998–1999. MMWR 1999;48:577–81.

FIGURE 3. Number of intussusception reports after the rhesus rotavirus vaccine-tetravalent (RRV-TV) by vaccination date — United States, September 1998–December 1999

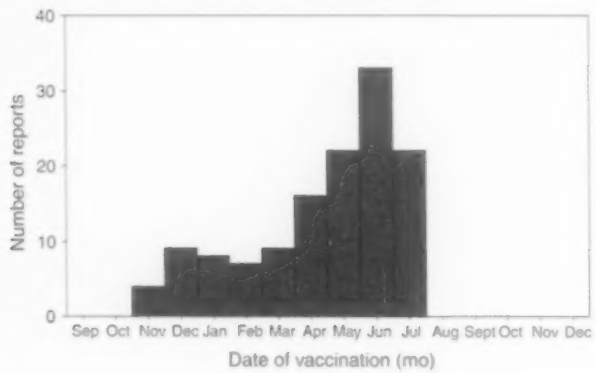


FIGURE 4. Number of intussusception reports after any vaccines, by vaccination date — United States, January 1991–December 1999

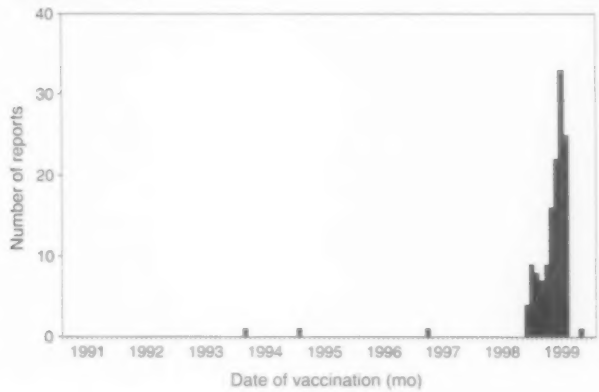
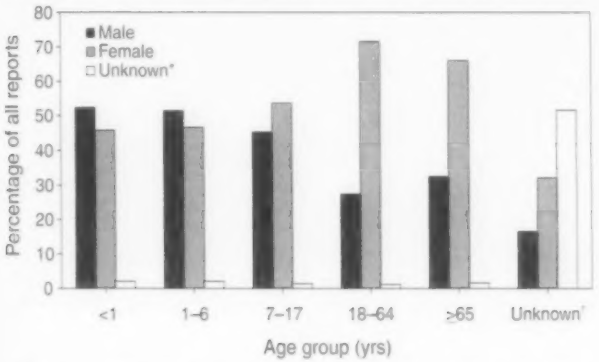
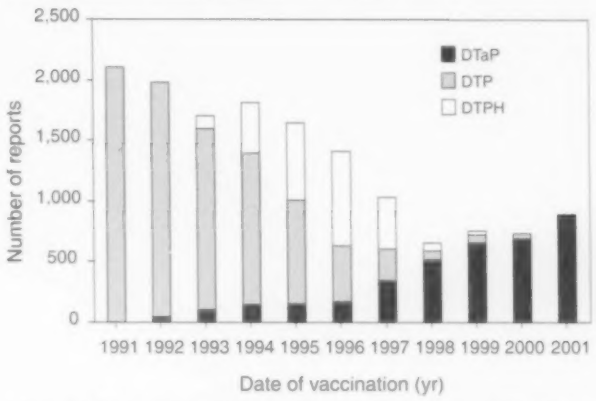


FIGURE 5. Reports of Guillain-Barré syndrome after influenza vaccination, by influenza seasons — United States, 1991–2001



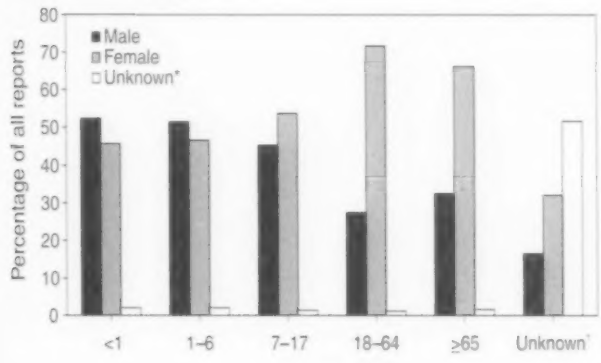
* Net doses distributed equals total doses distributed during the period, less returned doses.

FIGURE 6. Reports of fever after DTaP,* DTP,† or DTPH§ vaccination — United States, 1991–2001



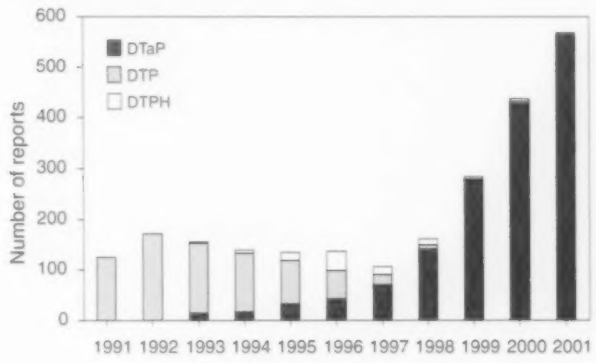
* Diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed.
† Diphtheria and tetanus toxoids and pertussis vaccine adsorbed.
§ Diphtheria and tetanus toxoids and pertussis vaccine adsorbed and *Haemophilus* b conjugate vaccine (diphtheria CRM197 protein conjugate).

FIGURE 7. Reports of febrile seizure and other convulsive disorders after DTaP,* DTP,† or DTPH§ vaccination — United States, 1991–2001



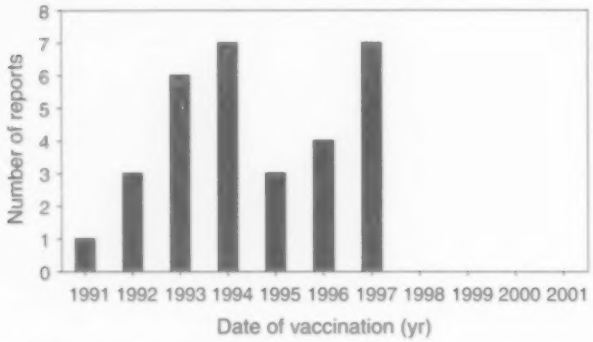
* Diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed.
† Diphtheria and tetanus toxoids and pertussis vaccine adsorbed.
§ Diphtheria and tetanus toxoids and pertussis vaccine adsorbed and *Haemophilus* b conjugate vaccine (diphtheria CRM197 protein conjugate).

FIGURE 8. Reports of injection-site edema after fourth and fifth doses of DTaP,* DTP,† or DTPH§ vaccination — United States, 1991–2001



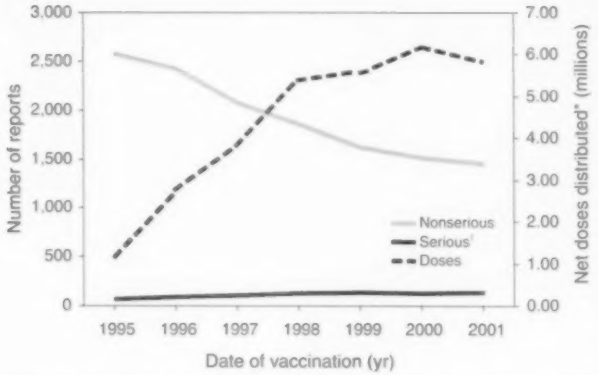
* Diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed.
† Diphtheria and tetanus toxoids and pertussis vaccine adsorbed.
§ Diphtheria and tetanus toxoids and pertussis vaccine adsorbed and *Haemophilus* b conjugate vaccine (diphtheria CRM197 protein conjugate).

FIGURE 9. Reports of vaccine-associated paralytic poliomyelitis (VAPP) after OPV* vaccination — United States, 1991–2001†



*Oral poliovirus vaccine live trivalent.
†No VAPP case after inactivated poliovirus vaccine during 1991–2001 was reported to the Vaccine Adverse Event Reporting System.

FIGURE 10. Reports of adverse events after varicella vaccination — United States, 1991–2001



*Net doses distributed equals total doses distributed during the period, less returned doses.
†According to the regulatory definition, serious adverse events involve hospitalization or prolongation of hospitalization, death, or reported life-threatening illness or permanent disability. Food and Drug Administration. 21 CFR Part 600.80. Postmarketing reporting of adverse experiences. Federal Register 1997;62:52252–3.

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